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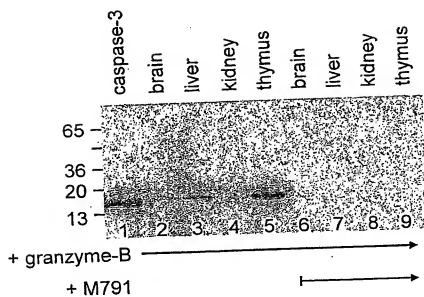


FIG.2A

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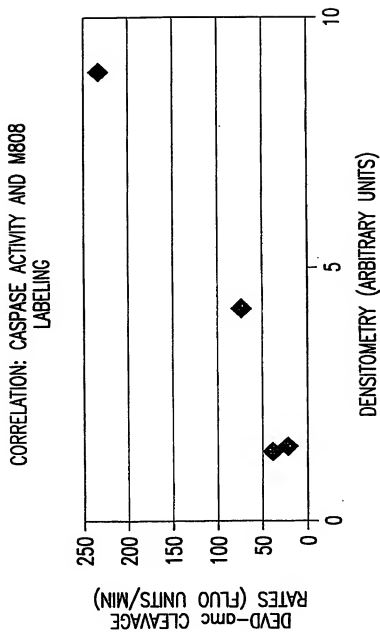


FIG.2B

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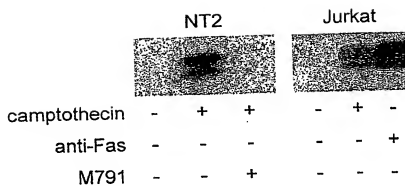


FIG.2C

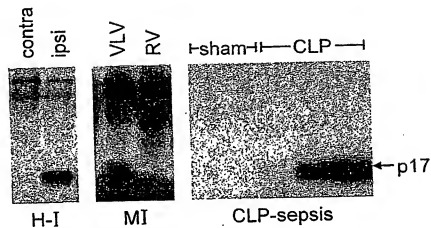


FIG.2D

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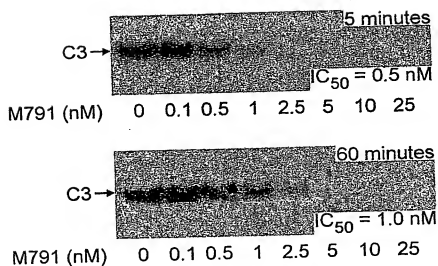


FIG.3A

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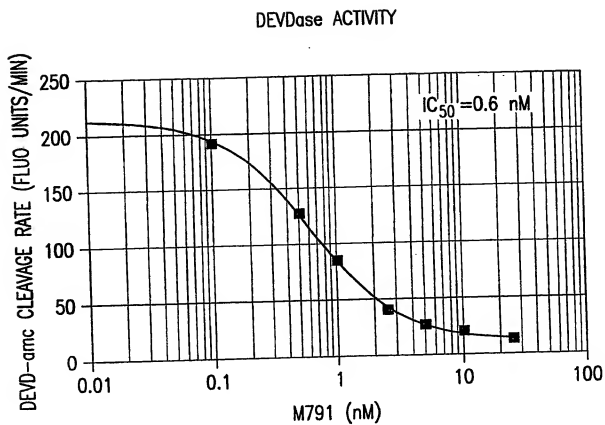


FIG.3B

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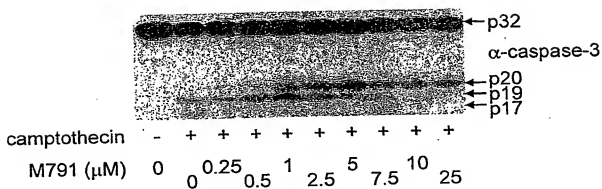


FIG.4A

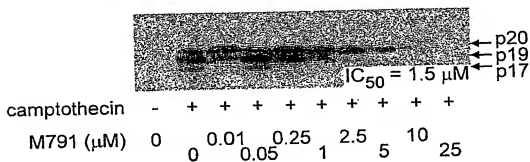


FIG.4B

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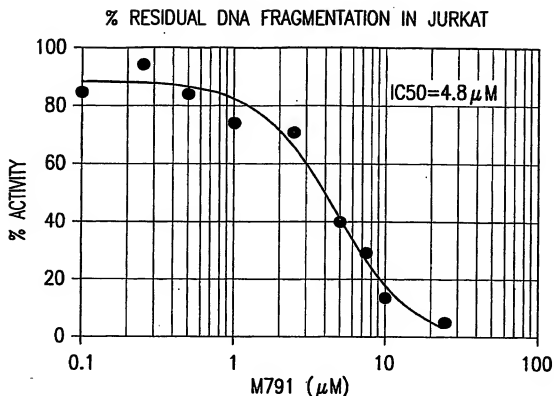


TABLE II. COMPARATIVE POTENCIES OF CASPASE INHIBITORS MEASURED BY M808 AND DNA FRAGMENTATION

| CELL LINE  | INHIBITOR | IC <sub>50</sub> PROBE ( $\mu$ M) | IC <sub>50</sub> DNA CLEAVAGE ( $\mu$ M) |
|------------|-----------|-----------------------------------|--|
| NT2        | M791      | 0.5                               | 0.4                                      |
| NT2        | M826      | 0.045                             | 0.03                                     |
| NT2        | M090      | 3.6                               | 7  |
| JURKAT     | M791      | 2.5                               | 4.8                                      |
| JURKAT     | M826      | 0.045                             | TO BE DETERMINED                         |
| THYMOCYTES | M826      | 0.07                              |  |
| THYMOCYTES | M867      | 0.09                              |  |

FIG.4C



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PCT/CA2004/000152

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- DETERMINE EXPECTED [ $^{125}$ I]-M808 SIGNAL IN DRUG-TREATED ANIMAL, BASED ON MEASURED TOTAL AMOUNT OF CASPASE-3, AS MEASURED BY WESTERN BLOT
- EXPECTED [ $^{125}$ I]-M808 SIGNAL: 3.6 UNITS
- ACTUAL [ $^{125}$ I]-M808 MEASURE: 1.0 UNIT
- FREE ENZYME =  $\frac{\text{ACTUAL/EXPECTED}}{= 1.0 \text{ UNITS}/3.6 \text{ UNITS}} = 0.28$   
= 28% FREE CASPASE ACTIVE SITES

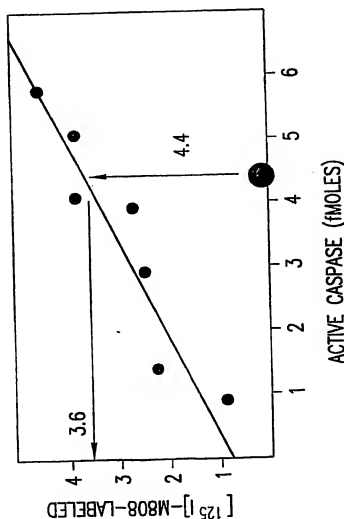


FIG. 5A

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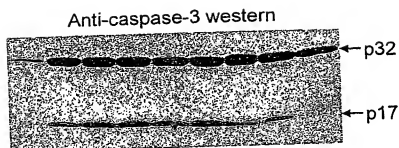
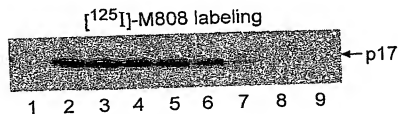


FIG.5B



| TABLE III. PERCENT OCCUPANCY OF CASPASE ACTIVE SITE BY M867 IN APOPTOTIC RAT THYMOCYTES |     |      |       |       |      |      |      |      |      |
|---|-----|------|-------|-------|------|------|------|------|------|
| LANE  | 1   | 2    | 3     | 4     | 5    | 6    | 7    | 8    | 9    |
| M867 CONCENTRATION ( $\mu$ M)   | 0   | 0    | 0.005 | 0.025 | 0.05 | 0.1  | 0.25 | 1    | 5    |
| p17 DENSITOMETRY  | 0.6 | 14.3 | 17.6  | 19.0  | 17.1 | 19.2 | 11.3 | 10.2 | 4.6  |
| EXPECTED 125I M808 SIGNAL*  |     |      | 52.7  | 56.9  | 51.4 | 57.6 | 34.0 | 30.6 | 13.9 |
| ACTUAL 125I M808 SIGNAL   | 4.7 | 42.6 | 42.8  | 40.4  | 39.1 | 28.4 | 11.9 | 3.7  | 0.0  |
| RATIO ACTUAL/EXPECTED   |     |      | 0.8   | 0.7   | 0.8  | 0.5  | 0.4  | 0.1  | 0.0  |
| % FREE ACTIVE SITES   |     |      | 81    | 71    | 76   | 49   | 35   | 12   | 0    |
| % OCCUPANCY   |     |      | 19    | 29    | 24   | 51   | 65   | 88   | 100  |

\* EXPECTED [<sup>125</sup>I]M808 SIGNAL CALCULATED BASED ON p17 DENSITOMETRY vs [<sup>125</sup>I]-M808 SIGNAL IN ABSENCE OF DRUG

FIG.5C

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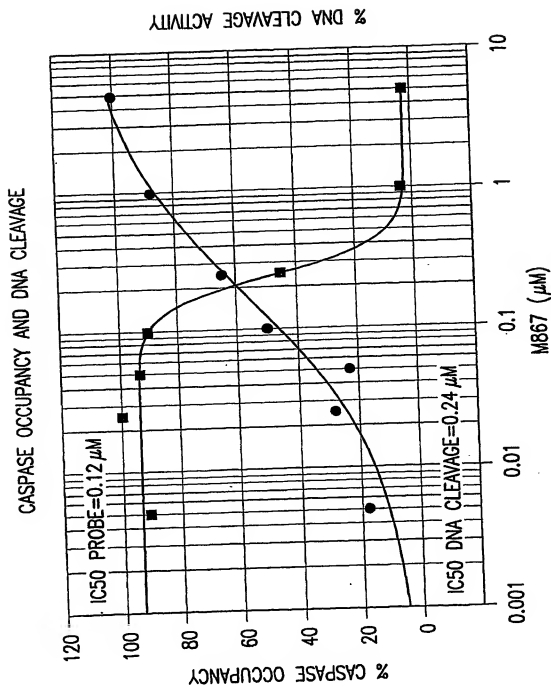


FIG.5D

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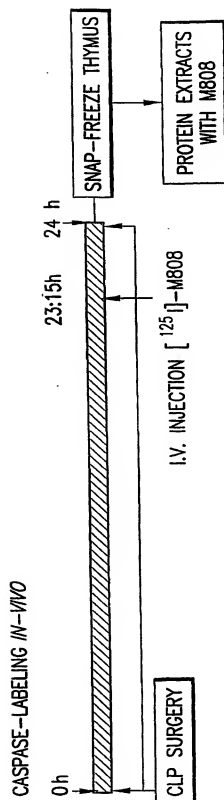


FIG.6A

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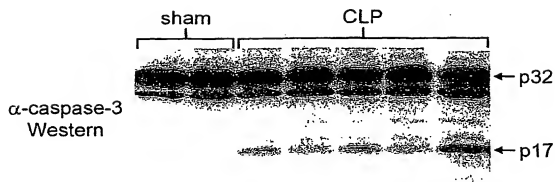


FIG.6B

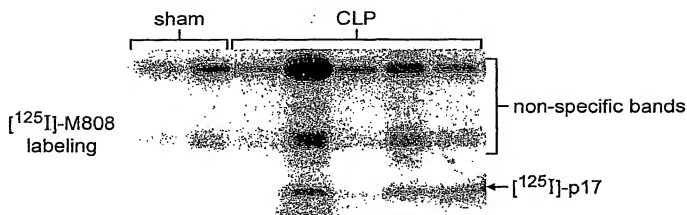


FIG.6C

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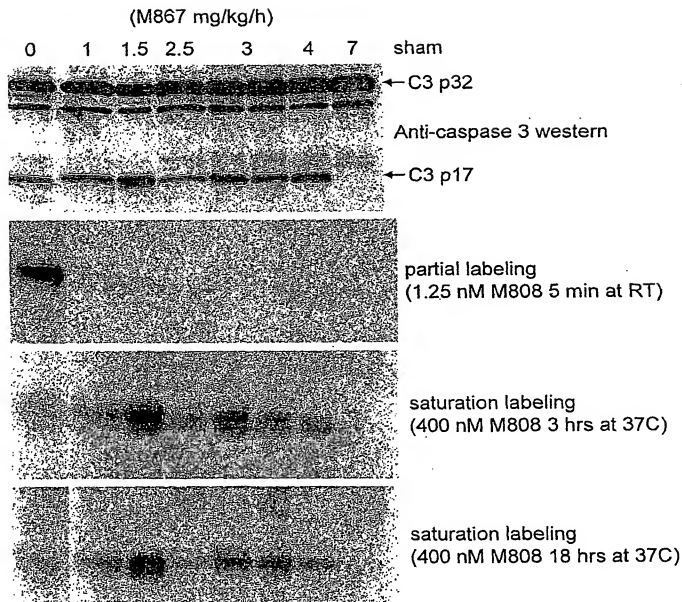


FIG.7

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